AR201-13782

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EASTMAN

May 21, 2002

Ms. Christine Todd Whitman, Administrator
U.S. EPA
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

RE: HPV Chemical Challenge Program, AR-201

Dear Ms. Whitman:

This letter is submitted by Eastman Chemical Company ("Eastman") in response to comments received from the Environmental Protection Agency ("EPA") dated April 18, 2002 following EPA's review of the test plan and robust summaries for 2-heptanone (CAS No.: 110-43-0). I would like to thank the EPA for its review and welcome the recognition of its completeness and fulfillment of Eastman's obligation to this chemical in the HPV program.

Below are the EPA's comments to various robust summaries and our responses:

Health Effects

1. *"Acute Toxicity.* Acute oral and inhalation toxicity tests in rats are adequate. The acute oral toxicity test in mice appears inadequate. The submitter needs to address the deficiencies noted in the robust summaries. No additional acute toxicity tests are needed."

The EPA has provided no rationale as to why the acute toxicity study in mice appears inadequate, and Eastman disagrees with this conclusion. The study in mice was conducted at the same time as that of the rat, and the data available and summarized was essentially identical. Therefore, Eastman believes that this study should be considered as adequate. The reliability of this study was deemed as "reliable with restrictions." This was the same reliability as the rat acute oral toxicity study that was deemed adequate.

2. *"Acute oral toxicity.* For both studies, the submitter needs to add, if available, all dose levels, and the number of animals at each dose. The submitter needs to clarify the LD_{50} for the acute oral toxicity test in mice because the result of the study stated no deaths noted at any dose."

Unfortunately, due to the date at which this study was completed (1964), the requested details are no longer available. Due to these study detail deficiencies, we graded the reliability of both studies as "reliable with restrictions." In regard to the mouse study in which no deaths were

noted at the highest dose (1,600 mg/kg), we have changed the robust summary to read "LD_{50} = >1,600 mg/kg."

3. *"Acute inhalation toxicity.* The submitter needs to add the method by which the test atmosphere was generated (e.g., as aerosol, vapor, etc.)."

The robust summary for this study has been modified to address the concerns over the method for generating the test atmosphere by noting that the animals were exposed to the test material in the form of a vapor.

4. *"Repeated-dose inhalation toxicity.* The submitter needs to clarify the three exposure groups, to add the method by which the test atmosphere was generated (e.g., as aerosol, vapor, etc.), and to specify the hematological, clinical chemistry, and urinalysis parameters assessed."

The robust summary has been changed to clarify the three exposure groups as the two test exposure levels plus the controls. The summary has been modified to address the concerns over the method for generating the test atmosphere by noting that the animals were exposed to the test material in the form of a vapor. The clinical chemistry parameters analyzed have also been added to the summary. The manuscript did not indicate that any hematological or urinalyses were performed. Blood and urine were collected solely for the purpose of metabolite identification and was so noted in the robust summary.

5. *"Repeated-dose oral toxicity.* The submitter needs to add the frequency of data collection (for clinical signs, body weight, and food and water intake), the specific hematology, clinical chemistry and urinalysis parameters that were examined, and the specific organs that were weighed or examined for gross and microscopic pathology."

The robust summary for this study has been modified to address the EPA's concerns.

6. *"Reproductive/Developmental Toxicity (inhalation).* Although the study is considered adequate, information missing from the robust summary includes: the method for generating the test atmosphere, the timing of exposure days in both sexes in relation to mating and gestation, the timing of final sacrifices with respect to gestation and lactation, and the maternal and paternal endpoints that were analyzed (including the specific organs weighed and examined histologically)."

The robust summary for this study has been modified to address the concerns over the method for generating the test atmosphere by noting that the animals were exposed to the test material in the form of a vapor. We have also provided more detail relative to the specific organs weighed and examined, and that exposure to females occurred through gestation.

Ecotoxicity

7. "The following information is missing from the acute fish robust summary: the test substance purity, number of fish tested, and concentrations tested."

The robust summary for this study has been modified to address the EPA's concerns. The primary reference for this study was obtained and the detail provided within it has also allowed us to change the study reliability score from "reliable with restrictions" to "reliable without restrictions."

Environmental Fate

8. *"Biodegradation.* The submitter needs to provide information on the source/concentration of the microbial inoculum, initial concentration of the chemical, and time required for 10% biodegradation to take place."

Information in regard to the source/concentration of the microbial inoculum and initial concentration of the chemical has been added to the summary. However, the time required for 10% biodegradation to take place is not a calculated endpoint in this assay.

9. *"Fugacity.* To estimate transport and distribution, the sponsor used the EPIWIN Level III model which provides estimated values as default inputs. EPA recommends using the EQC level III model from the Canadian Environmental Modeling Centre at Trent University, which allows full control of data inputs. This model can be found at the following Web address: http://www.trentu.ca/academic/aminss/envmodel/."

While the Agency recommends use of the above-mentioned model, it is important to point out that the model in EPIWIN is a direct adaptation of the EQC level III model developed by Dr. Donald Mackay and co-workers (Mackay et al., 1996a, 1996b; Mackay 1991). It is noted in the EPIWIN suite users guide that this model uses the same equations as Mackay's EQC Level III Fugacity model; however, it was adapted specifically for use in EPIWIN. Based on the conclusion drawn by the Agency that "All appropriate SIDS-level tests/estimations have been performed," we have left the robust summary for this endpoint as is.

Enclosed with this letter is a computer diskette containing the test plan and modified robust summaries in Adobe Acrobat (.pdf) format. The HPV registration number for Eastman Chemical Company is

Sincerely,

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Technical Associate

Enclosure